

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY VF

PCT

To:

Eingegangen 24. März 2005

see form PCT/ISA/220

DEHMEL & BETTENHAUSEN
Patentanwälte

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/007527

International filing date (day/month/year)
08.07.2004

Priority date (day/month/year)
10.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61P35/00, A61K45/00

Applicant
MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/EP2004/007527

IAP20 Received 10 JAN 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/007527

Box No. II Priority

1. ☐ The following document has not been furnished:

☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/007527

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 4-7

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 4-7
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/007527

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-3
	No: Claims	
Inventive step (IS)	Yes: Claims	1-3
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-3
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

10/564435

International application No.

PCT/EP2004/007527

IAP20 Rec'd PCT/PTO 10 JAN 2006

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 1.1. The question as to whether the claimed invention appears to be novel, to involve and inventive step or to be industrially applicable has not been and will not be the subject of an international preliminary examination (Article 34(4)(a)(I)(ii) PCT; see International Search Report) in respect of unsearched subject-matter (Article 17(2)(a) Rule 66.1(e) PCT).
- 1.2. Present claim 1 relates to an assay in which the translocation / colocalisation of APPL1 and APPL2 is used. "APPL1" and "APPL2" are internal designations which had no established meaning in the art at the time of the invention. In the light of the description said claim is interpreted as relating to proteins APPL and DIP13beta encoded by the sequences with EMBL accession numbers AF169797 and AY113704, respectively. Consequently, the search was restricted to and this opinion only covers methods relating to the use of said proteins.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.

- 1.1. Present application discloses a method to screen for anti-proliferative drugs, based on assaying the relocalisation of RabB5 effectors APPL1 and APPL2.
- 1.2. Reference is made to the following document:
 - D2: WO 01/20022 A (MAX PLANCK GESELLSCHAFT ; RENZIS STEFANO DE (DE); ZERIAL MARINO (DE);) 22 March 2001 (2001-03-22)
 - D3: EP-A-1 088 898 (MAX PLANCK GESELLSCHAFT) 4 April 2001 (2001-04-04)
 - D7: MITSUUCHI Y ET AL: "Identification of a chromosome 3p14.3-21.1 gene, APPL, encoding an adaptor molecule that interacts with the oncoprotein-serine/threonine kinase AKT2" ONCOGENE, BASINGSTOKE, HANTS, GB, vol. 18, 1999, pages 4891-4898, XP002965023 ISSN: 0950-9232
- 1.3. Documents D2 and D3 disclose methods for detecting anti-proliferative drugs based on assays for Rab5 effectors. D7 discloses that APPL interacts with AKT2,

which relocates in the cells under insulin stimulation.

None of the cited documents disclose that APPL1 or APPL2 interact with Rab5, nor that they are translocated within the cells upon EGF stimulation.

2. Novelty and inventive step

- 2.1. In the light of the prior art the technical problem can be seen as the provision of an alternative method for identifying anti-proliferative drugs.

The solution provided by the current application is the use of APPL1/APPL2 as target molecules and to monitor their translocation within cells treated with test compounds.

- 2.2. Claim 1 fails to meet the requirements of Article 6 and Rule 6 PCT in that the matter for which protection is sought is not clearly defined. The compounds "APPL1" and "APPL2" lack true technical features and are only identified by internal designations which had no established meaning in the art at the time of the invention and thus leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claim unclear.

In the light of the description said claim is interpreted as relating to proteins APPL and DIP13beta encoded by the sequences with EMBL accession numbers AF169797 and AY113704, respectively.

The prior art presently available to the IPEA neither discloses nor suggests a method for identifying anti-proliferative drugs by monitoring the relocalisation of APPL and DIP13beta.

- 2.3. Present claims 1-3, insofar as relating to APPL and DIP13beta would therefore appear to meet the requirements of Article 33(2)(3) PCT.

Further comment

- 1.1. The attention of the applicants is drawn to the fact that a reply to this opinion is only expected if they intend to file a chapter II demand.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/007527

- 1.2. If amendments are filed, the applicants must comply with the requirements of Rule 66.8 PCT and indicate the basis in the originally filed application of the amendments made (Art. 2(b) PCT), otherwise these amendments will not be taken into consideration for the establishment of international preliminary examination report.

The attention of the applicants is drawn to the fact that if the application contains an unjustified plurality of independent claims no examination of any of the claims will be carried out.

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